Rise in serum angiotensin 2 levels related to exercise

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The aim of this study is to find out at what moment in time during, or after, short high intensity or prolonged low intensity exercise there is a significant rise in serum AngII levels.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON37918

Source
ToetsingOnline

Brief title
Rise in serum angiotensin 2 levels related to exercise

Condition

- Other condition

Synonym
high blood pressure, -Hypertension

Health condition

Hypertensie

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: angiotensin 2, blood pressure, exercise

Outcome measures

Primary outcome

Serum angiotensin 2 levels before and after high and low intensity exercise.

Secondary outcome

ACE-genotyping

Blood pressure

Study description

Background summary

High blood pressure (hypertension) indicates the deterioration of the set points of metabolic fitness and is one of the most frequent metabolic risk factors in Western countries. A major target of the current pharmacological treatments involves the inhibition of the enzyme angiotensin-converting enzyme (ACE), which lowers the serum levels of the vasoconstrictor angiotensin II (AngII) and develops a generally positive effect on mortality. Based on only one study ACE inhibitors are now even considered to prevent sarcopenia and physical decline in the elderly. These recently voiced beliefs do not match the physiological effects that are found in humans. It has been identified that genetic and pharmacological inhibition of ACE activity can be detrimental for metabolic fitness and possibly strength in men. ACE inhibition can reduce cross section of muscle fibers and genetic inhibition of ACE can manifest in reduced trainability of aerobic fitness.
The negative impact of ACE inhibition on metabolic function in man may be explained by the *double* role of the product of ACE action, AngII, in vasoconstriction and capillary growth (angiogenesis). In resting muscle, the role of AngII is to restrict blood from entering non-active muscles. The AngII-mediated vasoconstriction is overridden with the onset of contraction through flow-induced dilatation of conduit arteries and arterioles and is expected to promote angiogenesis by activating the endothelial cell population that constitutes the capillary wall. Different studies support the notion that a switch in AngII action from arterioles to the endothelium of the perfused vessel lumen facilitates exercise-induced capillary growth in human skeletal muscle.

An interaction between physical activity and angiotensin 2-mediated angiogenesis may also explain the large differences in therapeutic efficiency of current anti-hypertensive treatment. Genotypic variants of ACE with lowered serum angiotensin 2 due to the presence of the *I-allele* which silences ACE expression show lowered gains in maximal oxygen uptake with exercise rehabilitation. Transcript expression of pro-angiogenic factors, which reflects the mechanism that instructs the elevation in muscle capillarity, after exercise is reduced in genotypes being homozygous (ACE-II) or heterozygous (ACE-ID) for the *I-allele*.

Awareness of the existence of such a mechanism could develop major economic and clinical repercussions on current Health Care practice. Pharmacological inhibition of AngII action may have undesirable side effects, particularly, in the situation when one wants to exploit the sympatholytic and angiogenic benefits of physical therapy. This activity-dependent mechanism has rarely been valued in pharmacological studies of hypertension

We aim to expose the pathway by which AngII is implicated in exercise-induced capillary growth of human muscle. We hypothesize that the blunting of AngII production with concomitant exercise reduces improvements in metabolic fitness by removing an important stimulus for capillary growth in exercised muscle.

Study objective

The aim of this study is to find out at what moment in time during, or after, short high intensity or prolonged low intensity exercise there is a significant rise in serum AngII levels.

Study design

The study is an cross-sectional study.

The subjects will perform an incremental exercise test, a low intensity exercise test and a high intensity exercise test on separate occasions. The later 2 tests will be performed in random order. The duration of the data collection phase will be approximately 3 weeks.

Study burden and risks

Subjects will visit the VU University Amsterdam on three separate occasions. Testing will take about an hour each time. The exercise tests will entail a degree of effort and fatigue but this will not be excessive or prolonged and is something that the participants will be able to go through. Participants will be constantly monitored before, during and after all tests and will be made aware that they may withdraw from the study at any time. An intravenous cannula will be inserted into a vein in the subjects arm for obtaining blood samples. This may cause a brief discomfort for some subjects. There is a small risk of infection when inserting the cannula. To minimize the risk, the cannula will be

inserted and the blood samples will be drawn by a qualified phlebotomist with the use of sterile equipment. In total eighteen 2 ml blood samples (six per test) per person will be withdrawn.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Age: 30 * 40 year
- Gender: male
- Caucasian

Exclusion criteria

- Taking medication which can interfere with the renin-angiotensin system (including ACE inhibitors)
- Unable to cycle
- Certain illnesses, impairments or disorders, which affect the renin-angiotensin system, physical activity level and/or physical condition (including persons with hypertension)

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-05-2012
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	03-04-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL38386.029.12